CD4⁺ T cells may help initiate the skin lesions, CD8⁺ T cells that produce type 1 cytokines (IFN-gamma) are responsible for the persistence of the lesions. This may explain the paradox observed in HIV infected patients in whom psoriasis (and PsA/reactive arthritis) can worsen dramatically even as CD4⁺ T-cell counts fall. In PsA patients a predominantly TH1 cytokine response is observed (increased IL2, TNF-beta, and IFN-gamma), but there is also an increased IL-10 response. It has recently been proposed, based on MRI studies, that PsA is enthesitis based disease, and that it is distinct from RA, where synovitis is the primary pathological feature. Local treatment of psoriasis with psoralens plus ultraviolet A radiation (PUVA) often results in long-standing remissions by greatly reducing the number of activated T cells in psoriatic skin due to induction of T-cell apoptosis. Methotrexate, and DAB389-interleukin-2 preferentially induce apoptosis of activated T cells in skin and other sites. On the other hand, cyclosporine A and topical corticosteroids only inhibits the production of cytokines; and psoriasis often recurs soon after the cessation of this treatment. Likewise, TNF-alpha blockade therapy has been found to be very effective in treating patients with severe psoriasis and PsA (including SpA), but the benefit is relatively short-lived after the therapy is discontinued. Administration of CTLA4Ig fusion protein (that blockades the B7-CD28/CD152 pathway of T cell costimulation) has produced a marked improvement of psoriasis in a phase I trial.

REFERENCES

- 1 Martinez-Borra GS, et al. *J Invest Dermatol.* 2000;**115**:824-8
- 2 Capon F, et al. *Mol Genet Metab.* 2000;**71**:250-5
- 3 Asumalahti K, et al. *Hum Mol Genet.* 2000;**12**:1533-42

Pain and memory of pain – Thursday 14 June, 14.00-15.30/Forum Hall

SP0034 PLASTICITY OF PAIN MODULATION DUE TO CHRONIC PAIN

D Bouhassira, N Danziger. *Physiopharmacologie Du Système Nerveux, INSERM U-161, Paris, France*

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Descending, propriospinal, and segmental modulatory systems, tonically or phasically inhibit or facilitate the spinal transmission of nociceptive signals. Although it is widely accepted that these endogenous modulatory systems affect sensations of pain, the way in which they are brought into play and their consequences on nociceptive behaviour have rarely been addressed in the context of tissue injury. An increase of tonic descending modulation has been demonstrated during the acute stage of inflammation in both electrophysiological and behavioural experiments suggesting that this enhanced descending inhibition may limit hyperalgesia during acute inflammation.¹

To analyse further the changes of pain modulatory systems under pathological conditions and determine their potential role in the pathophysiology of pain syndromes, we investigated in a recent series of electrophysiological studies in the rat the modulation of the spinal transmission of nociceptive information during the course of inflammation.

In a first series of experiments,² diffuse noxious inhibitory controls (DNIC), which are supraspinally mediated inhibitory

controls triggered by the application of noxious stimuli, were investigated at different stages during the development of adjuvant-induced monoarthritis in the rat. In the acute stage of monoarthritis (i.e., 24-48 h), the DNIC-induced inhibitions of nociceptive neurons produced by mechanical or thermal stimulation of the arthritic joint were significantly increased at all intensities by comparison with the normal joint. In contrast, in the animals with a chronic monoarthritis (i.e., 3-4 weeks), the DNIC-induced inhibitions were not different from those observed in control animals. These data suggested that chronic inflammatory processes might have induced a reorganisation of the spinal transmission of nociceptive signals and/or modulatory systems, which could modify the recruitment of DNIC.

To test these hypotheses, other experiments were designed to analyse the changes of tonic modulation acting on the spinal transmission of nociceptive information in rats with acute or chronic monoarthritis.³ Tonic descending inhibitions were analysed by comparing the electrophysiological properties of spinal convergent neurons with ankle input before and after spinalization. Tonic descending inhibition of convergent neurons with input from the inflamed ankle was enhanced during the acute stage and then decreased during the chronic stage of monoarthritis. In addition, changes in the spinal transmission of nociceptive signals were unmasked by removing descending modulation in animals with monoarthritis: sensitisation of spinal neurons with input from the inflamed ankle was demonstrated during the acute stage of monoarthritis, while a crossed transmission between inflamed and normal sides was observed during the chronic stage of the disease.

In conclusion, these studies showed dynamic and stage-dependent modifications of the spinal transmission and modulation of nociceptive information during the course of inflammation. During both acute and chronic stages of inflammation, descending controls tended to dampen central changes at the spinal level. Such a functional plasticity might play a significant role in the pathophysiology of some acute or chronic pain syndromes observed in humans: an imbalance of descending controls could exacerbate the consequences of the central changes induced by the inflammatory processes and could result in increased and persistent pain.

REFERENCES

- 1 Dubner R, Ren K. Endogenous mechanisms of sensory modulation. *Pain Suppl.* 1999;**6**:S45
- 2 Danziger N, Weil-Fugazza J, Le Bars D, Bouhassira D. Alteration of descending modulation of nociception during the course of monoarthritis in the rat. *J Neurosci.* 1999;**19**:2394-2400
- 3 Danziger N, Weil-Fugazza J, Le Bars D, Bouhassira D. Stage-dependent changes in the modulation of spinal nociceptive neuronal activity during the course of inflammation. *Eur J Neurosci.* 2001;**13**:230-40

SP0035 SUPRA-SPINAL MECHANISMS OF PAIN AND NON-INVASIVE IMAGING IN THE STUDY OF CHRONIC PAIN IN HUMANS

C Bushnell. *Anesthesia, McGill University, Montreal, Canada*

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Pain is a complex experience that includes sensory, emotional, autonomic and motoric components, and each of these components can differ among various pain states. Despite the many qualitative differences of clinical and experimental pain states, they all share a common aversive nature, leading us to characterise each as "pain." This talk will present evidence showing a